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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/599,760	06/22/00	NEWELL M	I0277/7009 H

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EXAMINER	
ZARA, I	
ART UNIT	**PAPER NUMBER**
1635	11

DATE MAILED: 07/12/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/599,760	Applicant(s) NEWELL, MARTHA K.	
	Examiner Jane Zara	Art Unit 1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-74 is/are pending in the application.

4a) Of the above claim(s) 1-59,65,73 and 74 is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 60-64 and 66-72 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

KATRINA TURNER
PATENT ANALYST

Attachment(s)

15) ☒ Notice of References Cited (PTO-892)
16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 4, 6 & 9 .
18) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other:

DETAILED ACTION

Claims 1-74 are pending in the instant application.

Election/Restriction

Applicant's election without traverse of Group VII, claims 60-64 and 66-72, in Paper No. 10 is acknowledged.

Claims 1-59, 65 and 73-74 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in Paper No. 10.

Claims 60-64 and 66-72 have been examined as indicated below.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 64 and 67 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

It is unclear from the claims whether the regulation of lysosomal pH is obtained upon the administration of a lysosomal UCP inhibitor (such as a dominant negative lysosomal UCP) in combination with a lysosomal targeted binding peptide or molecule, or alternatively upon the

administration of a lysosomal targeted binding peptide or molecule in the absence of a lysosomal UCP inhibitor.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 60-64 and 66-72 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claims are drawn to a method for regulating lysosomal pH in vitro or in vivo comprising the administration of inhibitors of lysosomal UCP. The claims are also drawn to the prevention and treatment of any and/or all infectious diseases in an organism comprising the regulation of lysosomal pH, comprising the administration of inhibitors of lysosomal UCP activity.

The following factors have been considered in determining that the specification does not enable the skilled artisan to make and/or use the invention claimed.

The state of the prior art and the predictability or unpredictability of the art. Bouillaud et al teach the expression of uncoupling protein (UCP) in brown adipose tissue, where UCP is known to uncouple mitochondrial respiration from ATP production by the introduction of

a proton conducting pathway through the mitochondrial inner membrane. Bouillard et al teach the generation of dominant negative mutants of UCP upon the mutation of amino acids which are essential for nucleotide inhibition of the proton transport in UCP (See especially the abstract, introduction and figure 7). Cone teaches the general motivation of uncoupling oxidative phosphorylation from ATP production in cancer cells in order to reduce the proliferative capacity of such tumor cells (See especially columns 2-5). Szoka et al teach the lysosomotrophic properties of weak bases such as chloroquine, monensin and PAMAM dendrimers in attempts to design polynucleotide delivery systems in combination with charge neutralization, membrane permeabilization and subcellular localization agents, which agents include lysosomal targeting agents (See especially abstract and columns 17, 18, 35 and 36). While the references cited above generally teach that the ability to alter the pH of subcellular compartments (including lysosomes) is routinely accomplished in the art, the ability to predictably regulate lysosomal pH, however, either by selectively targeting uncoupling agents such as those described by Bouillard et al or Cone, or by the administration of lysosomotrophic agents to cells, as described by Szoka et al, is currently not a routine matter in the art. Furthermore, no evidence has been provided in the instant specification that the predictable regulation of lysosomal pH is achieved upon inhibition of UCP function in lysosomes in vitro or in vivo.

The amount of direction or guidance presented in the specification AND the presence or absence of working examples. Applicants have not provided guidance in the specification toward a method of regulating lysosomal pH in cells in vitro or in vivo comprising

the administration of a lysosomal UCP inhibitor, nor of preventing or treating an infectious disease comprising the administration of a lysosomal UCP inhibitor. The specification teaches a shift in the expression of UCP from lysosomes and the mitochondria to the plasma membrane in MDR cells in vitro. The specification also teaches the induction of MDR cell death in vitro comprising the administration of tunicamycin and anti-UCP antibodies. The specification fails to teach the regulation of lysosomal pH in cells in vitro or in vivo comprising the administration of a UCP inhibitor and further whereby treatment or prevention effects are provided for any infectious disease in an organism. One skilled in the art would not accept on its face the examples given in the specification of the changes observed in subcellular expression of UCP in cells in vitro following the administration of tunicamycin as being correlative or representative of the successful regulation of lysosomal pH in cells in vitro or in vivo following the administration of UCP inhibitors and further whereby treatment or preventive effects are provided for infectious diseases in an organism upon the administration of UCP inhibitors in view of the lack of guidance in the specification and known unpredictability associated with the ability to predictably regulate lysosomal pH in cells in vitro or in an organism comprising the administration of UCP inhibitors. The specification as filed fails to provide any particular guidance which resolves the known unpredictability in the art associated with the *in vivo* delivery of UCP inhibitors and treatment effects provided by the administration of such inhibitors to an organism, and specifically regarding the instant compositions and methods claimed, which treatment and preventive methods are for any and/or all infectious diseases or conditions.

The breadth of the claims and the quantity of experimentation required. The breadth of the claims is very broad. The claims are drawn to a method for regulating lysosomal pH in vitro or in vivo comprising the administration of inhibitors of lysosomal UCP. The claims are also drawn to the prevention and treatment of any and/or all infectious diseases in an organism comprising the regulation of lysosomal pH, comprising the administration of inhibitors of lysosomal UCP activity. The quantity of experimentation required to practice the invention as claimed would require the *de novo* determination of accessible target sites, modes of delivery and formulations to target appropriate cells and /or tissues harboring lysosomal UCP activity, such that lysosomal pH is predictably regulated in vitro and in vivo upon the administration of UCP inhibitors, and further that treatment and preventive effects are provided for any and/or all infectious diseases in an organism. Since the specification fails to provide any particular guidance for the regulation of lysosomal pH in vitro or in vivo comprising the administration of inhibitors of lysosomal UCP activity, nor for the successful treatment or prevention of any infectious diseases or conditions in an organism, and since determination of these factors for a particular UCP inhibitor is highly unpredictable, it would require undue experimentation to practice the invention claimed.

Conclusion

Certain papers related to this application may be submitted to Art Unit 1635 by facsimile transmission. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)). The official fax telephone numbers for the Group are (703) 308-4242 and (703) 305-3014. NOTE: If Applicant *does* submit a paper by fax, the original signed copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Jane Zara** whose telephone number is **(703) 306-5820.** If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John LeGuyader, can be reached on (703) 308-0447. Any inquiry regarding this application should be directed to the patent analyst, Katrina Turner, whose telephone number is (703) 305-3413. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

JZ

July 9, 2001

ANDREW WANG
PRIMARY EXAMINER